IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	: Peter Richardson	Art Unit	: 1623
Serial No.	: 10/537,564	Examiner	: Lawrence E. Crane, Ph.D.
Filed	: August 28, 2006	Conf. No.	: 4551
Title	: USE OF SPONGOSINE FOR THE TREATMENT OF PAIN		

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION OF PETER RICHARDSON UNDER 37 CFR § 1.132

Peter Richardson declares as follows:

1. I have BA in Biochemistry from the University of Oxford (1976), a MA from the University of Oxford (1979) and a Ph.D. in Biochemistry from the University of Cambridge (1979). My *curriculum vitae* is attached.

2. I am an inventor of the above-captioned patent application.

3. I supervised a study which found that spongosine can reduce inflammatory and neuropathic pain in animals at a dose of 0.4 mg/kg. I also supervised a study which found that spongosine can reduce diabetic neuropathic pain in humans at a dose of 0.1mg/kg. These results are completely unexpected because the dosages used result in a peak maximum plasma concentration of about 0.2 micromolar, an order of magnitude below the Kd for spongosine at the A2A adenosine receptor (about 2.0 micromolar). One would expect that at a plasma concentration so far below the Kd of spongosine for the A1 and A2A adenosine receptors, spongosine would not activate either receptor and thus would not have an analgesic effect. Also, surprisingly, additional studies using animal models of inflammatory and neuropathic pain

found that maintained plasma concentrations of 0.02 micromolar (i.e., 1% of the value required to activate A2A receptors in tissues) are effective in reducing pain.

4. Without being bound by any particular theory, it appears that in certain tissues, such as epithelia, tissue damaged by physical, chemical or biological trauma, and those tissues undergoing an inflammatory response, the pH is lower than that of other tissues. The lower pH alters the binding affinity of spongosine for adenosine receptors such that spongosine is selective for the A2A adenosine receptor in such tissues. This allows the unexpected alleviation of pain and inflammation by spongosine at a plasma concentration that is too low to activate A1 and A2A adenosine receptors in other tissues thereby avoiding such negative side-effects as bradycardia and hypotension respectively.

5. All statements made herein of my own knowledge are true and all statements made on information and belief are believed to be true; and further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the instant patent application or any patent issued thereon.

Date: 19/Dec/2009

Peter Richardson, Ph.D.

Curriculum Vitae of Dr Peter Richardson

Professional Profile

A highly respected professional with proven leadership skills and 20 years broad experience in drug discovery and development, with experience in CNS, cardiovascular, metabolic and anti-inflammatory therapeutic areas. Experience in both academia and industry has generated a sound understanding of the theory and practice of drug discovery and development. After discovering a new approach to the treatment of diabetic vascular disease and chronic inflammation (targeted adenosine A2A agonists), founded a small pharmaceutical company (CBT) with colleagues from Pfizer/Parke Davis, negotiated support from both pharmaceutical and academic parent organisations, raised venture capital funding and provided the investors with an exit by assisting the sale of the company to Biovitrum AB. After becoming Head of Discovery for Biovitrum, responsible for strategic development of the company's drug discovery efforts in three sites in Sweden and the UK. In this role also responsible for assessing in-licensing candidates (particularly the scientific basis of such opportunities) as well as expanding the knowledge and skill basis of the R&D organisation. Successful in aligning financial, research, and technical activities with long-term strategic business objectives.
Over the last ten years demonstrated an ability to manage organisational change while contributing to the co-ordination of all R&D activities from exploratory to clinical, as well as the ability to recruit and lead a company of dedicated scientists. A strong believer in encouraging the professional development of staff.

Current Position and Responsibilities

Nov 09 - present

Director, Grantabio

Founder and Director of Grantabio a group of experienced pharmaceutical scientists advising clients on the scientific basis of drug discovery and development. This ranges from company and programme evaluation through portfolio design, project management and IP maintenance as well as guidance in business development. Assistance, both short and long term, in the identification and implementation of specific disciplines (biology, medicinal chemistry and informatics) is also offered when required.
Advice on the out-sourcing of specific aspects of the drug discovery and development process is offered, as well as the evaluation of portfolios, in-licensing opportunities and in the sale/partnering of programmes.
Responsible for assisting clients in the evaluation of their portfolios with a focus on risk management, and in the evaluation of new in-licensing candidates including assessment of potential development strategies, costs and timelines. Assisting clients in assembling dossiers for out-licensing and company sales.

Previous Position and Responsibilities

May05 - Dec09

Vice President Drug Discovery Biovitrum AB (Stockholm, Sweden) and Managing Director and CSO, Cambridge Biotechnology Ltd (CBT, Cambridge, UK)

Responsible for leading CBT after the merger with Biovitrum AB, establishing a new research site in Cambridge, implementation of research programmes, and for liaison between CBT and the R&D sites in Stockholm and Goteborg. Joined the Biovitrum R&D Leadership Team which was responsible for drug development within the company's financial constraints as well as the co-ordination of research, preclinical development and clinical operations.
During this period a total of ten molecules in five different programmes were developed for toxicity testing in Stockholm, 80% of which were from the Cambridge site. Maintained the sustainable nature of CBT portfolio which has underpinned the recent sale of CBT.

Employment History

Jan 07 - Dec 09

Head of Discovery, Biovitrum AB (Stockholm, Sweden) and Managing Director and CSO, Cambridge Biotechnology Ltd (CBT, Cambridge, UK)

Responsible for the direction of approximately 100 scientists in the Stockholm, Goteborg and Cambridge discovery sites, with a combined budget of approximately £10M p.a. During this period the small Goteborg site was closed while the Stockholm site was supported in a new leaner and more efficient organisation. Joined the Biovitrum Management Team which was responsible for all aspects of the direction and governance of Biovitrum AB. Became an integral part of the teams assessing potential in-licensing opportunities, as well as being deeply involved in the out-licensing of programmes. Increased the scientific foundation of the company by expanding academic networks in the UK and Sweden and explained the Company R&D strategy to investors and stock market analysts. In 2008 the Discovery section of the R&D organisation in Biovitrum was successfully downsized. Subsequently Biovitrum adopted a new strategy which led to the complete abandonment of small molecule research in the company; this in turn led to the sale of the Cambridge site to Proximagen in late 2009.

May 02 - May 05

Company Director and Chief Scientific Officer, Cambridge Biotechnology Ltd, (Cambridge, UK)

Responsible for the scientific progress of CBT focusing on two novel programmes. The first was developed in the University of Cambridge and exploits the anti-inflammatory potential of the adenosine A2A receptor. The second from the University of Aberdeen developed the first small molecule agonist of the leptin receptor. Despite the novel nature of these programmes, the former has completed a successful Phase 2a trial while the latter is currently ready for GLP toxicity testing. Oversaw the development of a sustainable and risk balanced R&D portfolio focused on delivering preclinical candidates in a cost effective manner.

Oct 89 - Mar 07

Lecturer and Senior Lecturer, Department of Pharmacology, University of Cambridge (Cambridge, UK)

Taught and examined at all levels in the University, from first year undergraduates to PhD students. The research focused on the development of new approaches to the treatment of Parkinson's Disease (compounds from Kyowa Hakko and Schering Plough currently in Phase 3 and 2 respectively), the development of single cell gene expression analysis (a programme not maintained by Biovitrum AB) and the use of low tissue pH to focus the action of adenosine A2A receptor agonists (lead compound currently in Phase 2). Total research funding raised was approximately £2.3M between 1981 and 2001 with more than 70 refereed publications and assorted book chapters, abstracts etc.
Employed as a consultant to Kyowa Hakko (1995-2000; Parkinson's Disease) and Parke Davis/Pfizer (1997-2001; single cell gene expression).
Co-founder of Cambridge Biotechnology Ltd (CBT) in 2001 with colleagues from Parke Davis/Pfizer, and the raising of Venture Capital funding to establish a company of up to 35 employees. Given 5 years unpaid leave by the University of Cambridge to pursue this venture. Resigned from the University in 2007 to progress a career in the Pharmaceutical Industry.

Summary of qualifications

	Qualification	*Awarding Body*
1976	BA (Biochemistry)	University of Oxford
1979	MA	University of Oxford
1979	PhD (Biochemistry)	University of Cambridge